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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/916,140 08/21/97 SCOTT

M CIET-P04-203

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HM12/0913

EXAMINER

SCHNITZER, R

ART UNIT

PAPER NUMBER

1632

DATE MAILED:

09/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

08/916,140

Applicant(s)

SCOTT ET AL.

Examiner

Richard Schnizer

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 July 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 61-77 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 61-77 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 20.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

Two information disclosure statements and an amendment were received and entered as Paper Nos. 20, 22, and 24 on 2/5/01, 6/21/01, and 7/5/01, respectively. New claims 74-77 were added as requested. Claims 61-77 are pending and under consideration in this Office Action.

Rejections Withdrawn

The rejection of claims 62-73 under 35 USC 112, first paragraph are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claims 62 and 72-75 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed, invention for the reasons of record applied to claims 62, 72, and 73 in Paper No. 16.

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Claims 62 and 72-75 are drawn to methods wherein agents are added to a cell having a patched loss of function phenotype in order to identify agents which reverse the patched loss of function phenotype.

The specification discloses at page 20, lines 28 and 29, an assay in which agents are added to a cell which lacks functional patched gene product, and the ability of the cell to reproduce functional patched gene product is determined. There is no other support for the claimed method in the specification. However, the claimed method encompasses a variety of other methods which do not require the production of a functional patched gene product. Because patched is part of signaling pathway, mutations in other pathway proteins can interfere with the ability of patched to exert its function, and would therefore cause a patched loss-of-function phenotype. The specification fails to contemplate the use of such cells in the claimed method. Further, the claims encompass methods of identifying agents which reverse patched phenotype by duplicating patched function in ways other than the production of functional patched gene product, *i.e.* by stimulating or inhibiting the function of the pathway at a point downstream of patched. However, the specification fails to contemplate any method of restoring patched function to a cell lacking that function other than by reproducing functional patched protein in the cell. For this reason the scope of the claim which extends beyond ameliorating patched function by means of adding an agent which reproduces functional patched protein constitutes new matter.

At page 7 of the response filed 7/5/01, Applicant argues that "the description need only describe in detail that which is new or not conventional", citing page 1106, column 1 of the

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Guidelines for the Examination of Patent Applications. This does not relieve Applicant of the obligation to provide support for claim amendments. The issue here is not whether an existing description of the invention is adequate to convey possession. The issue is whether or not any description exists at all. Applicant has failed to point to any place in the specification that supports the claimed invention. When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure. See MPEP 2163.06. In this case, the appreciation by Applicant that mutations in other pathway genes may be important in oncogenesis does not amount to contemplation of the claimed method. For these reasons the rejection is maintained.

Enablement

Claims 61-77 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of identifying agents which affect patched-dependent signal transduction, does not reasonably provide enablement for methods of identifying agents which are inhibit the proliferation of cells, or which are useful for treating patients. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims, for the reasons of record applied to claims 61-73 in Paper No. 16.

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Claims 61, 62, and 74 are drawn to methods for identifying an agent for ameliorating an effect of loss of function of a patched gene in a cell. When read in light of the specification, the scope of these claims includes cells *in vivo*. The specification teaches no purpose for performing this method *in vivo* other than for the therapy of disorders characterized by a loss-of-function of a patched gene. Claims 63-73, 76, and 77 are drawn to methods of identifying agents for modulating proliferation in a cell *in vivo* or *in vitro*. Claim 75 is drawn to a method of identifying an agent for ameliorating an effect of a loss of function of a patched gene in a cell, with the additional step of administering the identified compound to "a patient". Claim 77 also requires administration of an identified agent to a patient. The specification does not teach administration of an agent to a patient for any purpose other than therapy of a disorder characterized by a loss-of-function of a patched gene. For these reasons, to fully enable these claims for their entire breadth, the specification must teach how to treat a patient with a disorder characterized by a loss-of-function of a patched gene.

As discussed in Paper No. 16, at the time of the invention, further basic research was needed in order to establish whether or not it was possible to affect cell growth *in vivo* or *in vitro* through the administration of agents intended to mimic the effects of patched. See Gailani et al (1997) as cited in Paper No. 16. The methods of claims 63-73, 76, and 77 represent the first steps in this research. However, the selection of agents to be tested in the claimed methods is problematic because the biochemical role of patched in cellular proliferation was not well understood at the time of filing. See Pennisi (Science 272:1583-1584, especially last sentence on

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page 1583). This necessitates further research is required before potential cell proliferation modulators can even be selected. See Pennisi, page 1584, column 3, last two paragraphs. Guidance in the specification as to the selection of agents to be tested is limited to the definition of "agents" as "preferably small organic compounds having a molecular weight of more than 50 and less than 2500 Daltons, and a non-limiting exemplary list of classes of molecules including peptides, saccharides, fatty acids, steroids, purines, and pyrimidines. Thus there is reason to doubt that the instant invention can be used to identify compounds which can modulate cell proliferation, and there is insufficient guidance as to what candidate compounds should be used in the method.

Even if the claimed methods could be used to successfully identify cell proliferation modulators in vitro, the development of such agents into drugs which can achieve therapeutic benefit in patients is highly unpredictable. It is well established in the art that drugs which are discovered by in vitro assays are not necessarily useful for in vivo applications. A variety of issues must be contemplated in moving from in vitro to in vivo applications, including bioavailability of the drug, toxicity of the drug, pharmacokinetics, drug metabolism and clearance, and potential drug interactions. Furthermore factors such as age, health, sex, and species of patient also affect the metabolism and performance of drugs in unpredictable ways. See Kato (1993) as cited in Paper No. 16.

At page 8 of the response filed 7/5/01, Applicant asserts that the specification provides extensive support for the identification of agents useful in the treatment of animals. This assertion

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is unpersuasive because it is unsupported by evidence or argument. Applicant has not addressed the portion of the rejection directed to *in vitro* uses of the invention. For these reasons the rejection is maintained.

It is suggested that the claims should be amended to recite methods of identifying agents which affect patched-dependent signal transduction, if explicit support for this use can be found in the specification.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 103-306-5441. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is usually in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached at 703-305-6608. The FAX numbers for art unit 1632 are 703-308-4242, and 703-305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Patsy Zimmerman whose telephone number is 703-308-8338.

Richard Schnizer, Ph.D.


ROBERT A. SCHWARTZMAN
PRIMARY EXAMINER